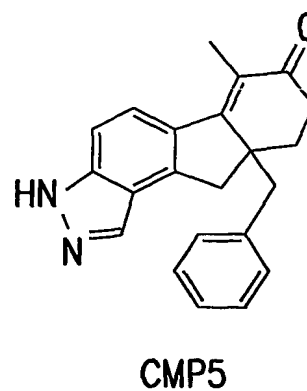
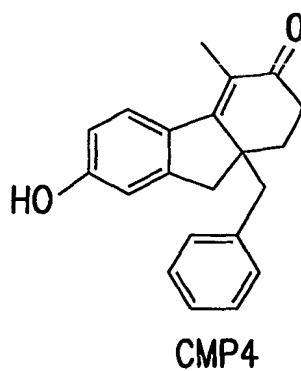
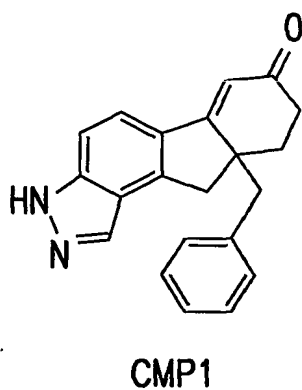
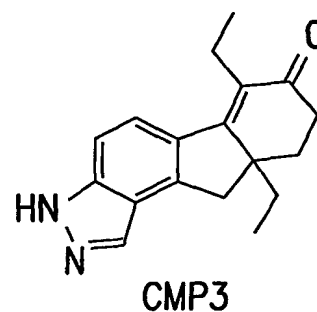
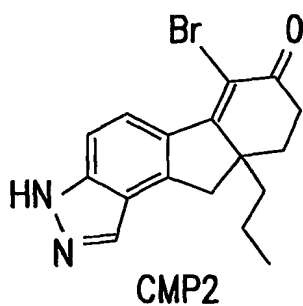
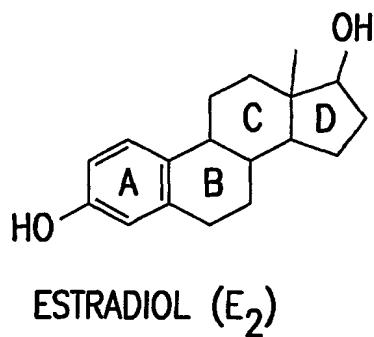


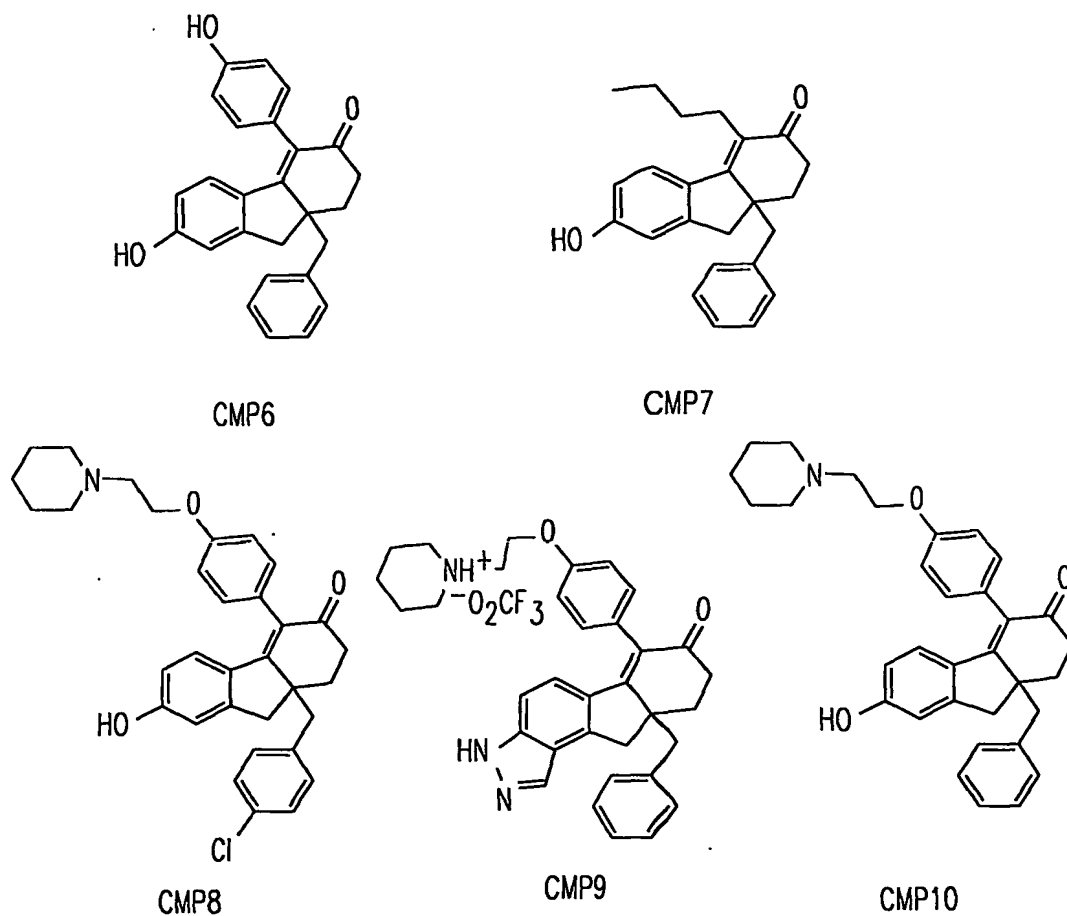
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| COMPOUNDS | BINDING (IC ₅₀ , nM) | | | | | |
|----------------|---------------------------------|-------------------|-------------------------------|---------------------------------------|---|---|
| | hER α wt | hER β wt | GST- ER α wt-LBD | GST- ER α LBD L(384)M | GST- ER α LBD L(384)M/ M(421)I | GST- ER α LBD L(384)M/ M(421)G |
| E ₂ | 1.6 | 1.4 | 2.3 | 5 | 0.7 | 46 |
| CMP2 | 676 | 6 | 800 | 48 | 42 | ND |
| CMP3 | 223 | 4 | 780 | 45 | 68 | ND |
| CMP1 | >10000 | >10000 | >10000 | >10000 | ND | 3900 |
| CMP4 | 1470 | 506 | 2320 | 1480 | ND | 12 |
| CMP5 | >10000 | 1247 | >10000 | >10000 | ND | 155 |

FIG.1A

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| | BINDING (IC ₅₀ (nM)) | | | | SELECTIVITY | | |
|-------|---------------------------------|---------------------------|--------------|-------------|-------------------|--------------------------|-------------------------|
| | GST-ER MG-LBD | GST-ER α wt-LBD | hER α | hER β | wt-LBD/ MG-LBD | hER α / MG-LBD | hER β / MG-LBD |
| CMP6 | 29 | 1371 | 223 | 96 | 47 | 7.7 | 3.3 |
| CMP7 | 25 | 1306 | 259 | 307 | 52 | 10.4 | 12.3 |
| CMP8 | 29 | 4436 | 1085 | 2232 | 153 | 37.4 | 77 |
| CMP9 | 107 | 1126 | 622 | 125 | 11 | 5.8 | 1.2 |
| CMP10 | 22 | 1272 | 375 | 184 | 58 | 17 | 8.4 |

FIG.1B

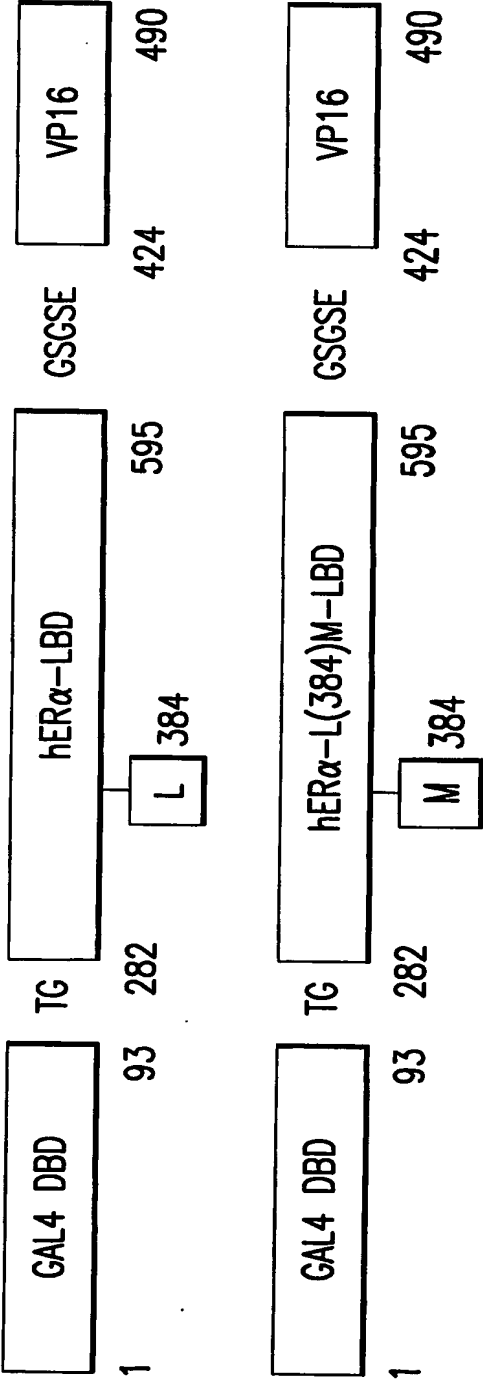


FIG.2A

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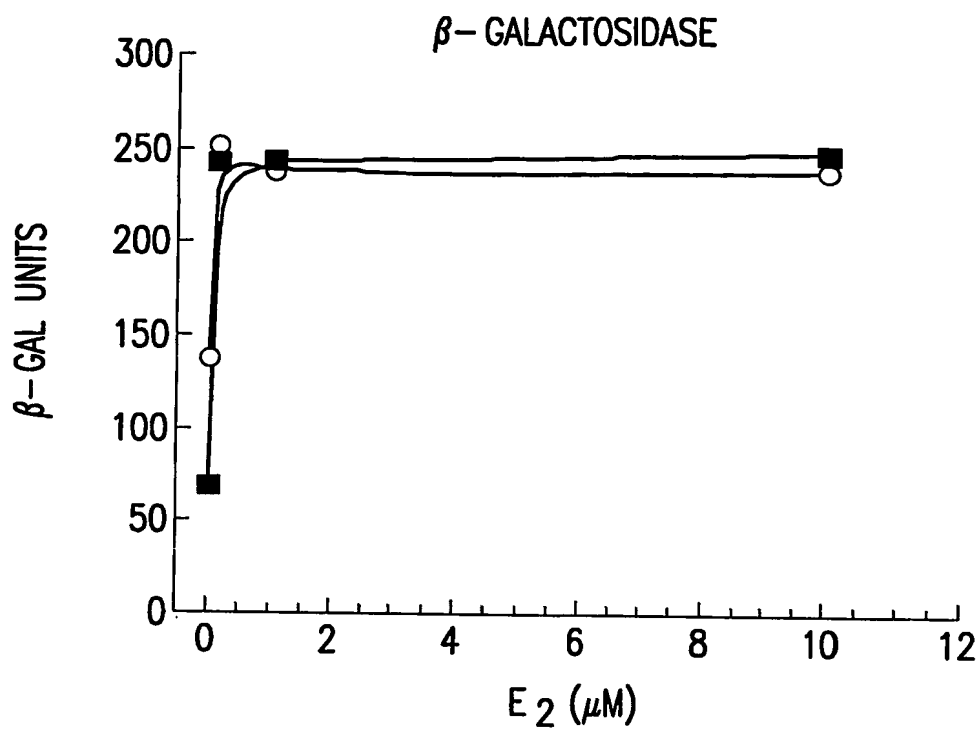


FIG.2B

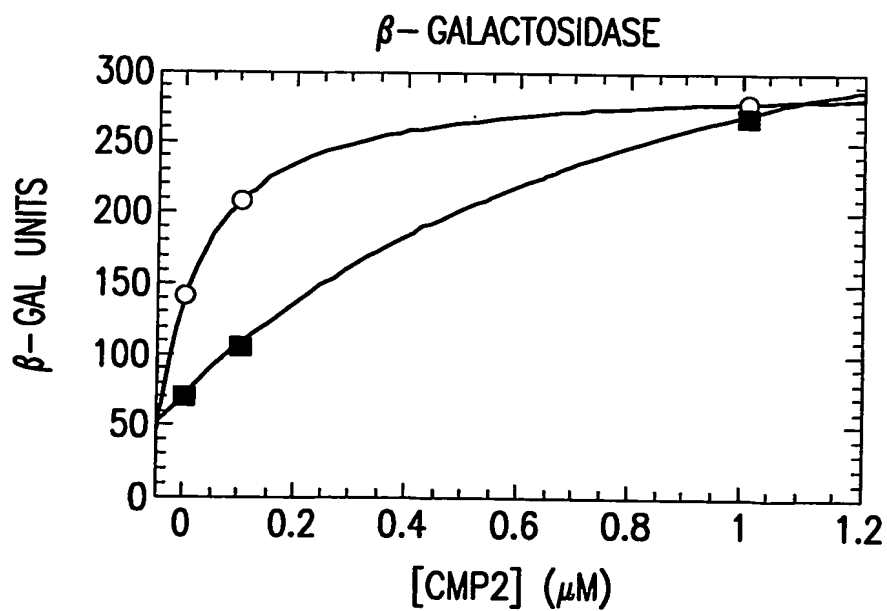


FIG.2C

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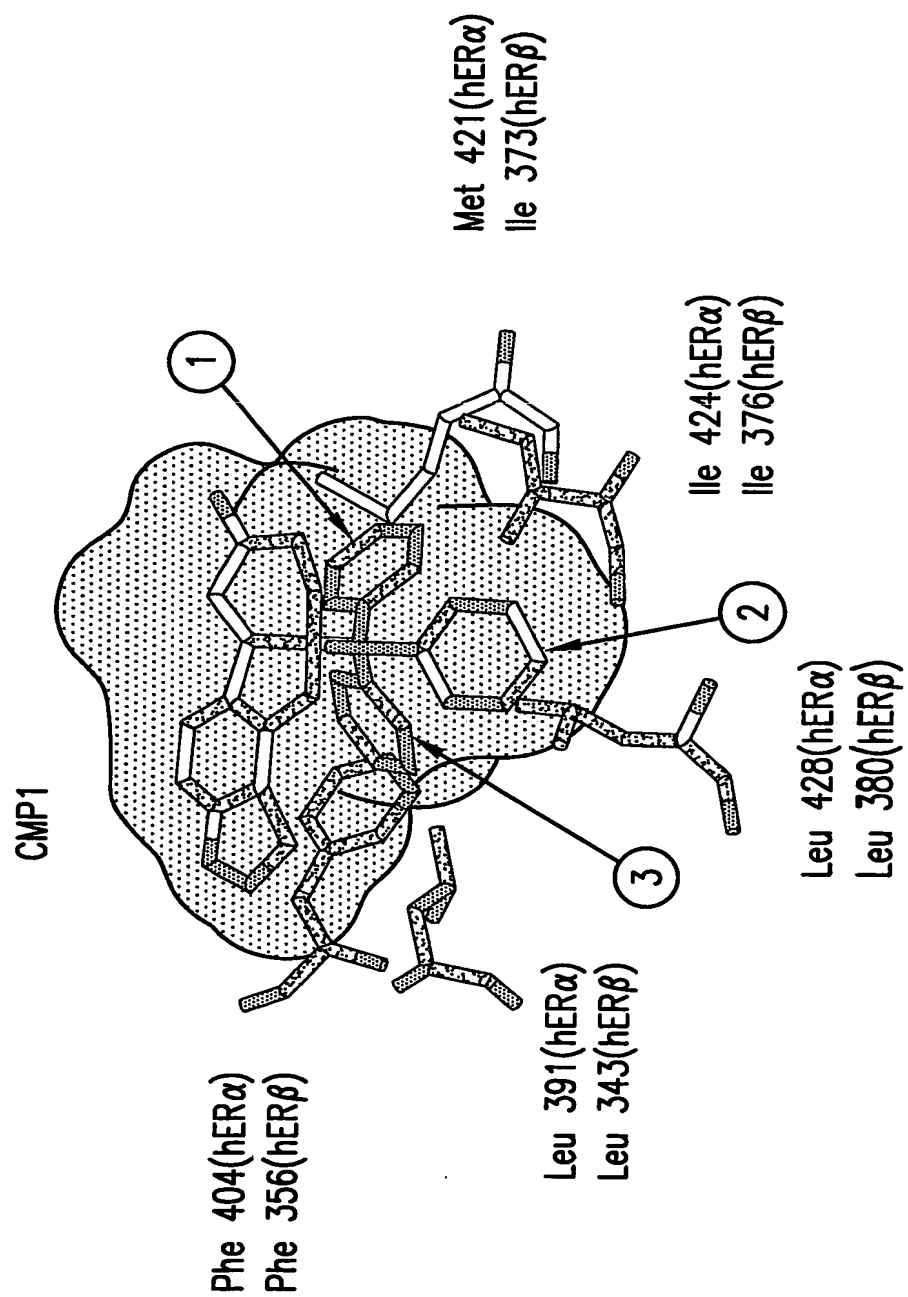


FIG.3

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| #CLONES | L391 | F404 | M421 | I424 | L428 | SEQ ID NO |
|---------|------|------|------|------|------|-----------|
| 5 | L | F | G | I | L | 3 |
| 2 | L | W | G | I | L | 4 |
| 9 | L | F | G | M | L | 5 |
| 2 | L | W | G | M | L | 6 |
| 1 | M | W | G | M | L | 7 |
| 11 | L | F | G | V | L | 8 |
| 2 | L | W | G | V | L | 9 |
| 1 | I | F | G | V | L | 10 |
| 5 | L | F | G | L | L | 11 |
| 3 | L | W | G | L | L | 12 |
| 1 | V | W | G | L | L | 13 |
| 1 | L | W | A | L | L | 14 |
| 1 | V | W | A | L | L | 15 |

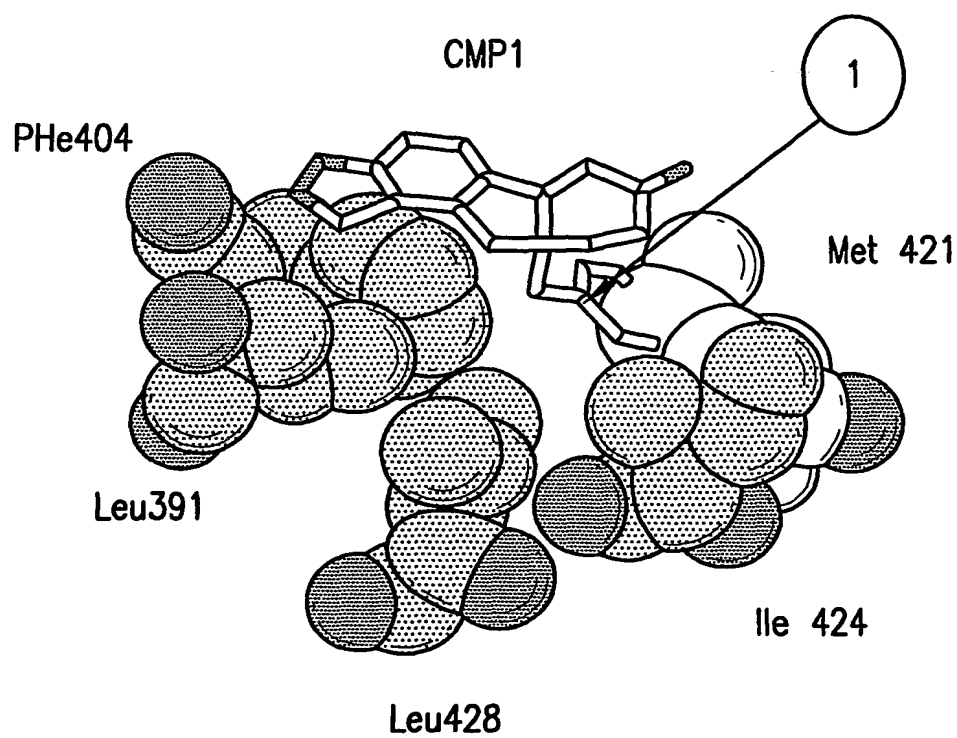


FIG.4

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CMP5

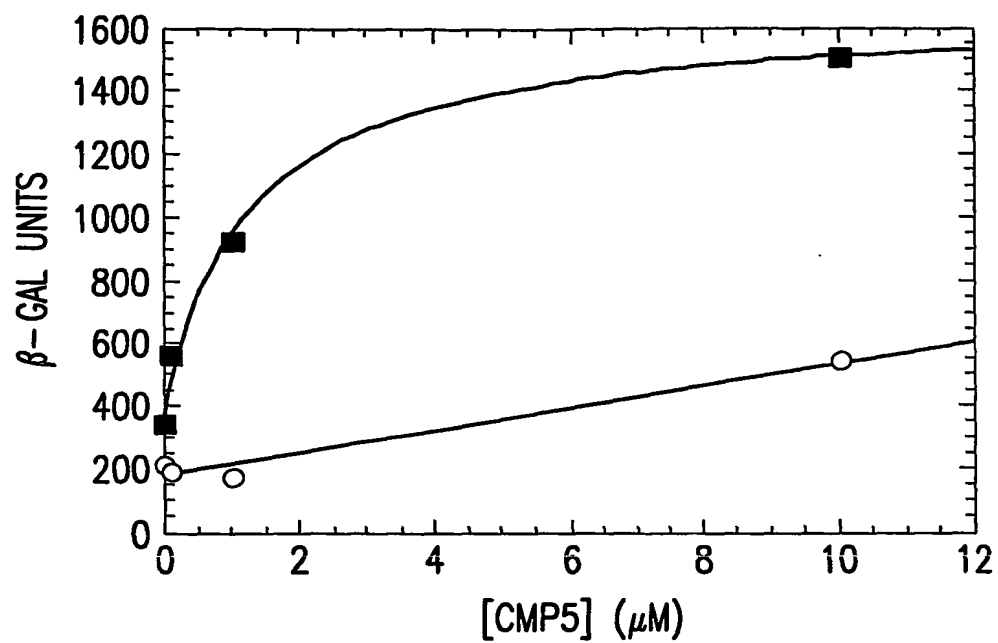


FIG.5A

CMP4

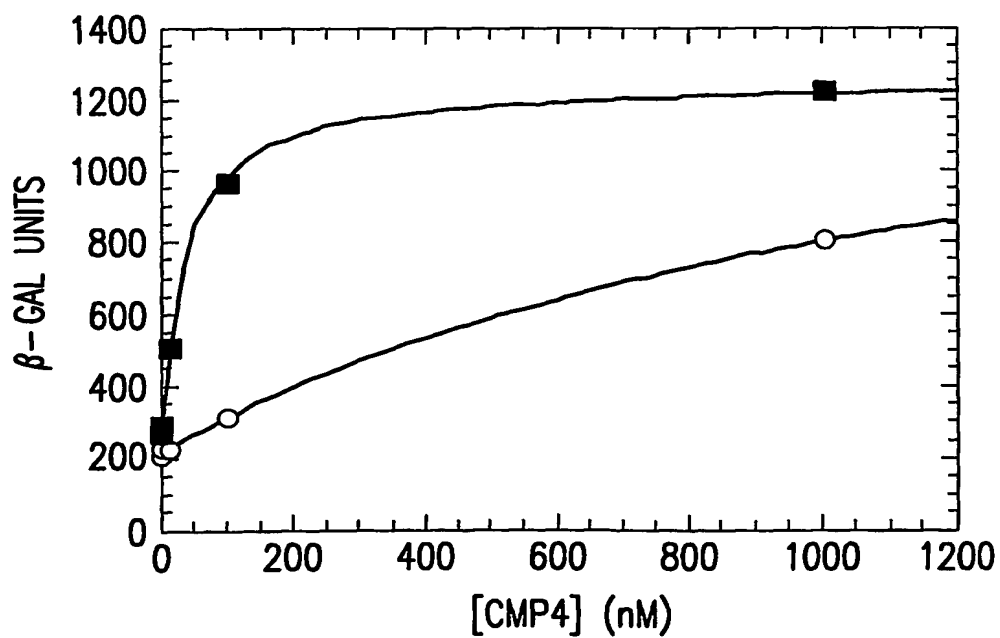


FIG.5B

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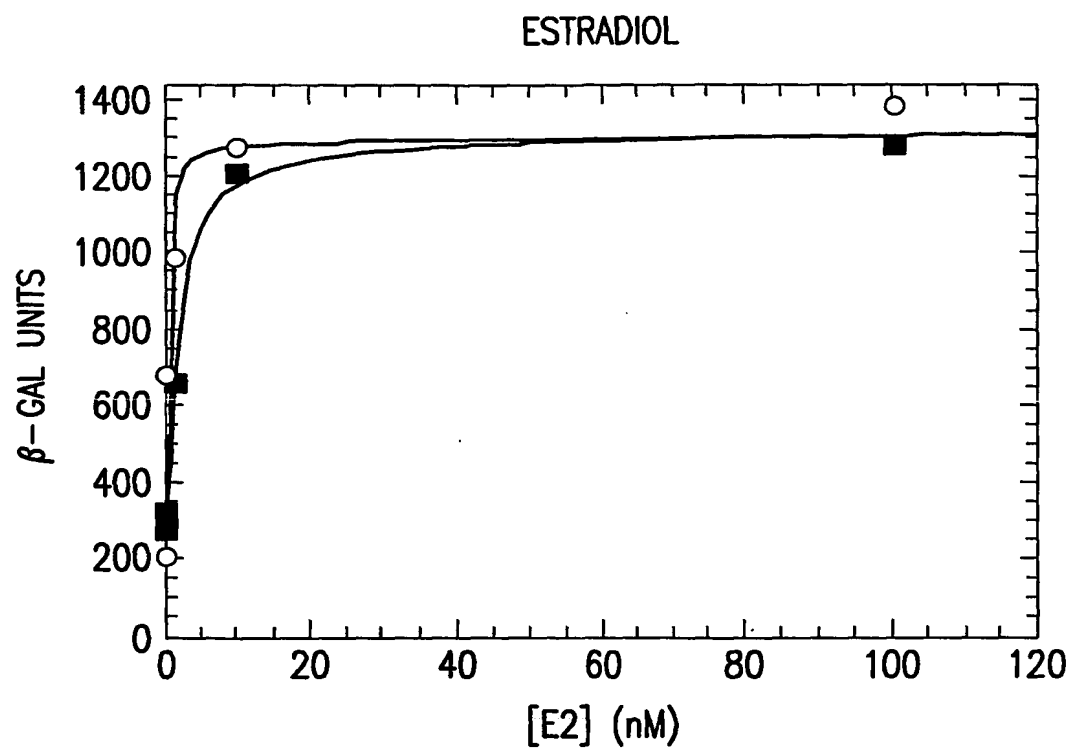


FIG.5C

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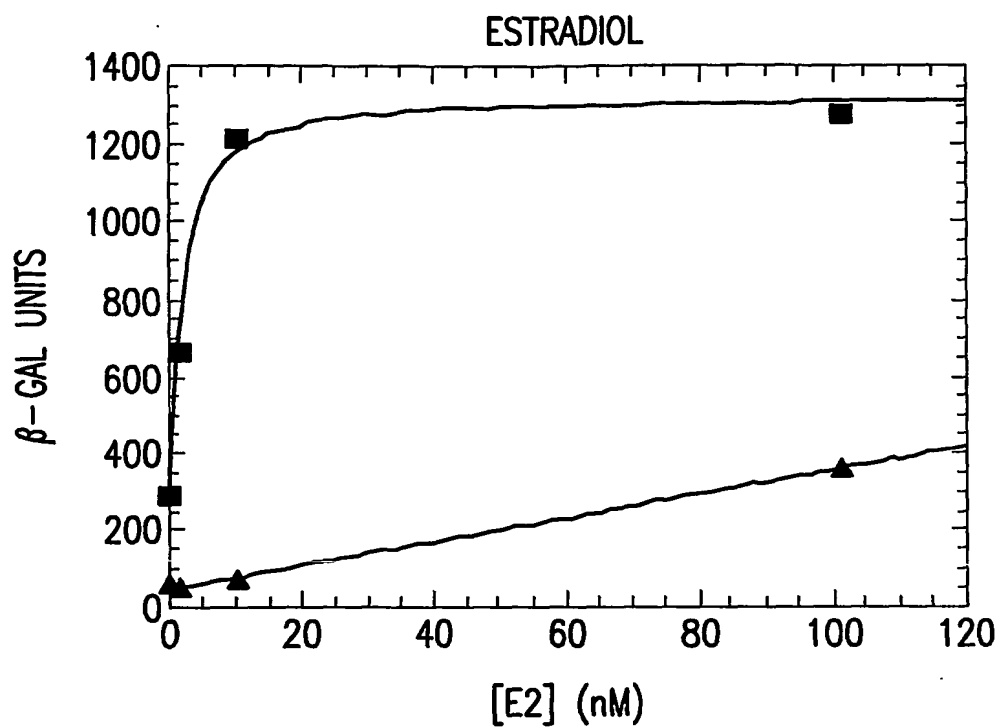


FIG.6A

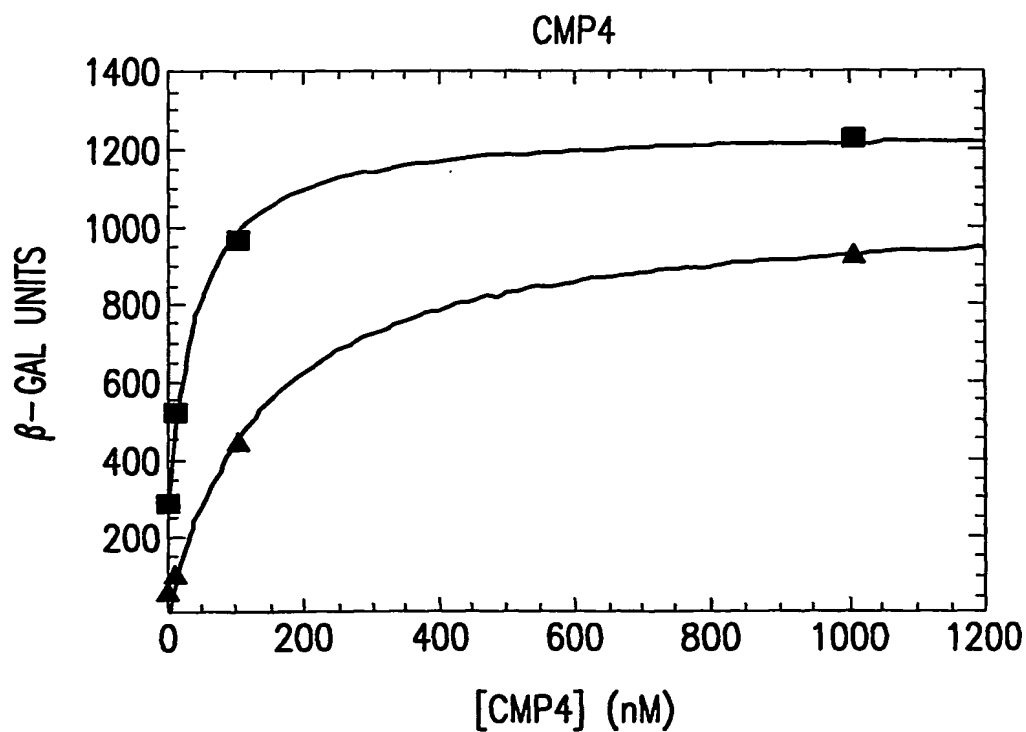


FIG.6B

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| [CMP4] (nM) | +D(351)A | | -D(351)A | |
|----------------|-----------------------|--------------------|-----------------------|--------------------|
| | β -GAL UNITS | FOLD- INDUCTION | β -GAL UNITS | FOLD- INDUCTION |
| 0 | 9 | - | 126.3 | - |
| 10 | 18.9 | 2.1 | 311.3 | 2.5 |
| 100 | 361.8 | 40.2 | 1,285.5 | 10.2 |
| 1,000 | 1,251.8 | 139 | 1,612.4 | 12.8 |
| 2,000 | 1,329.7 | 147.7 | 1,640.7 | 13 |

FIG. 7A

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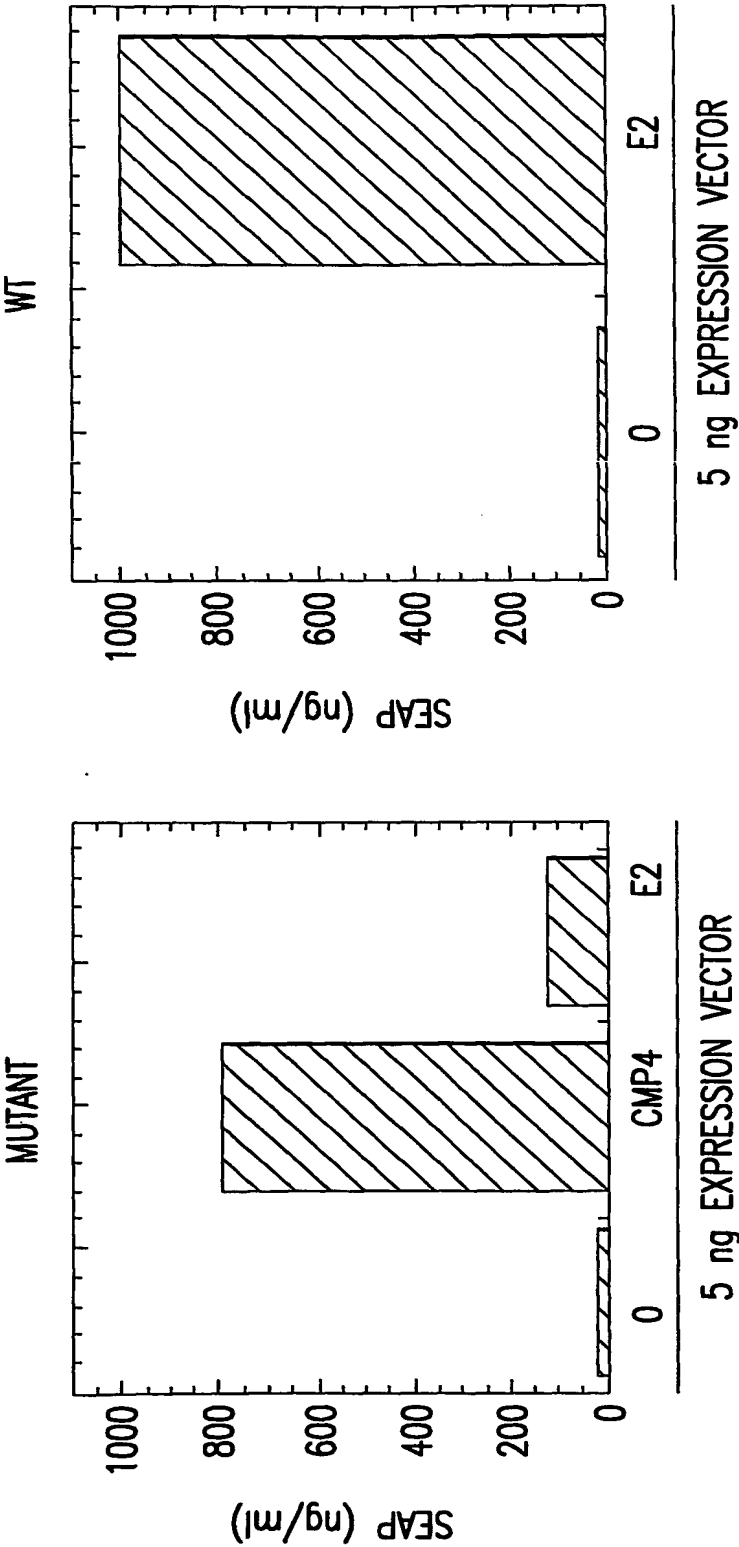


FIG.7B

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4-OH TAMOXIFEN

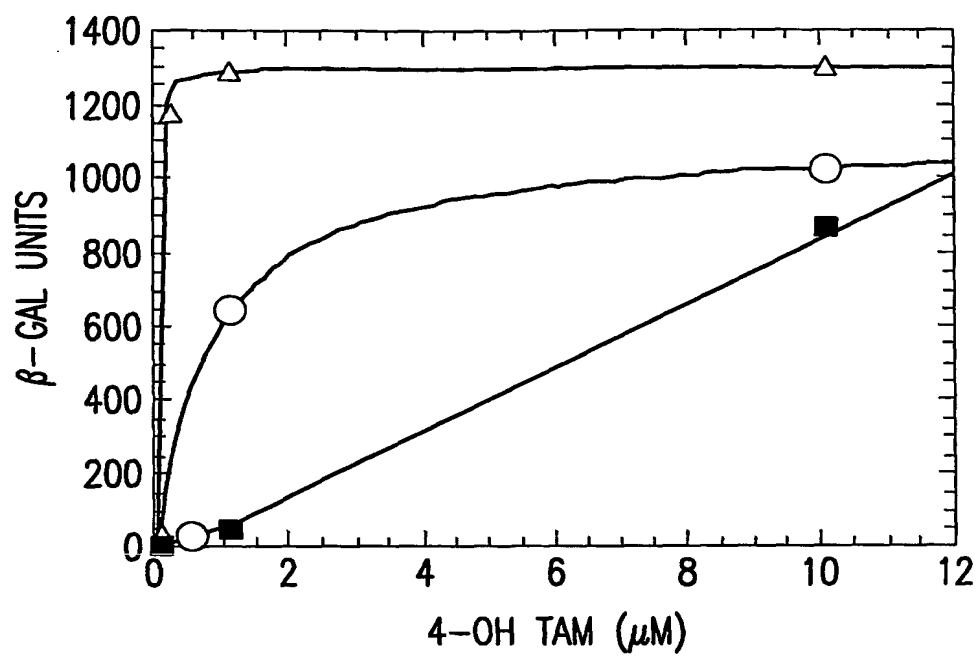


FIG.8A

CMP6

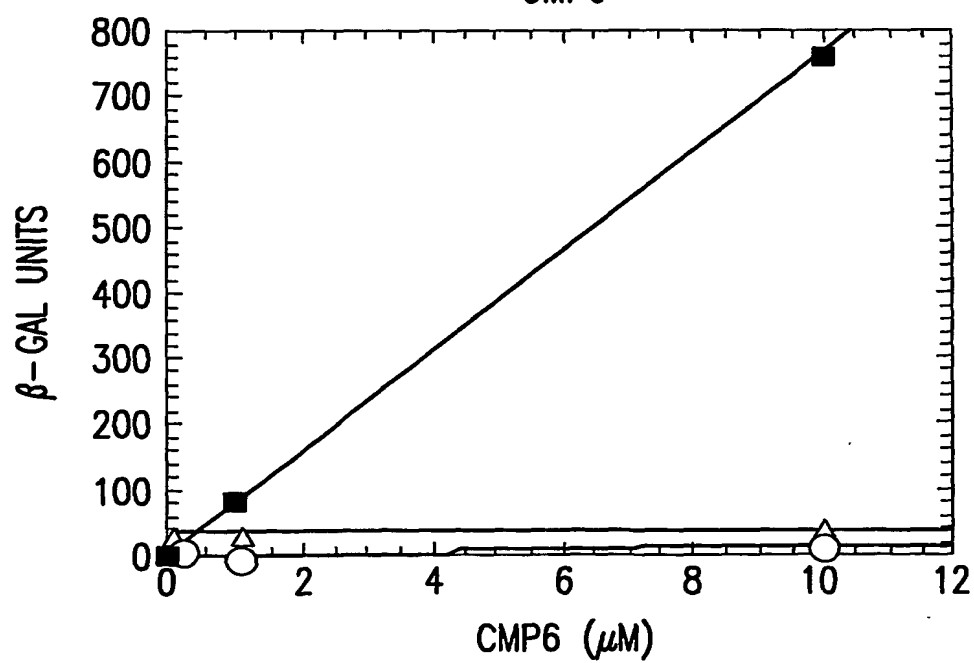


FIG.8B

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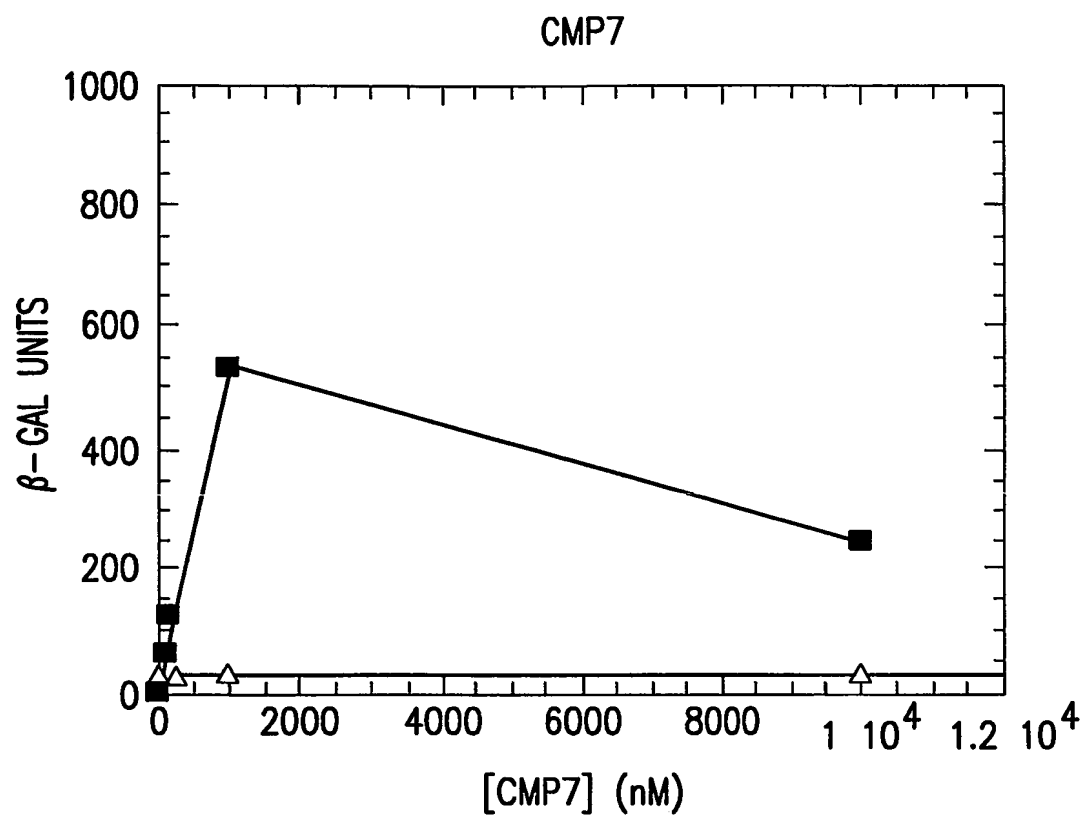


FIG.8C

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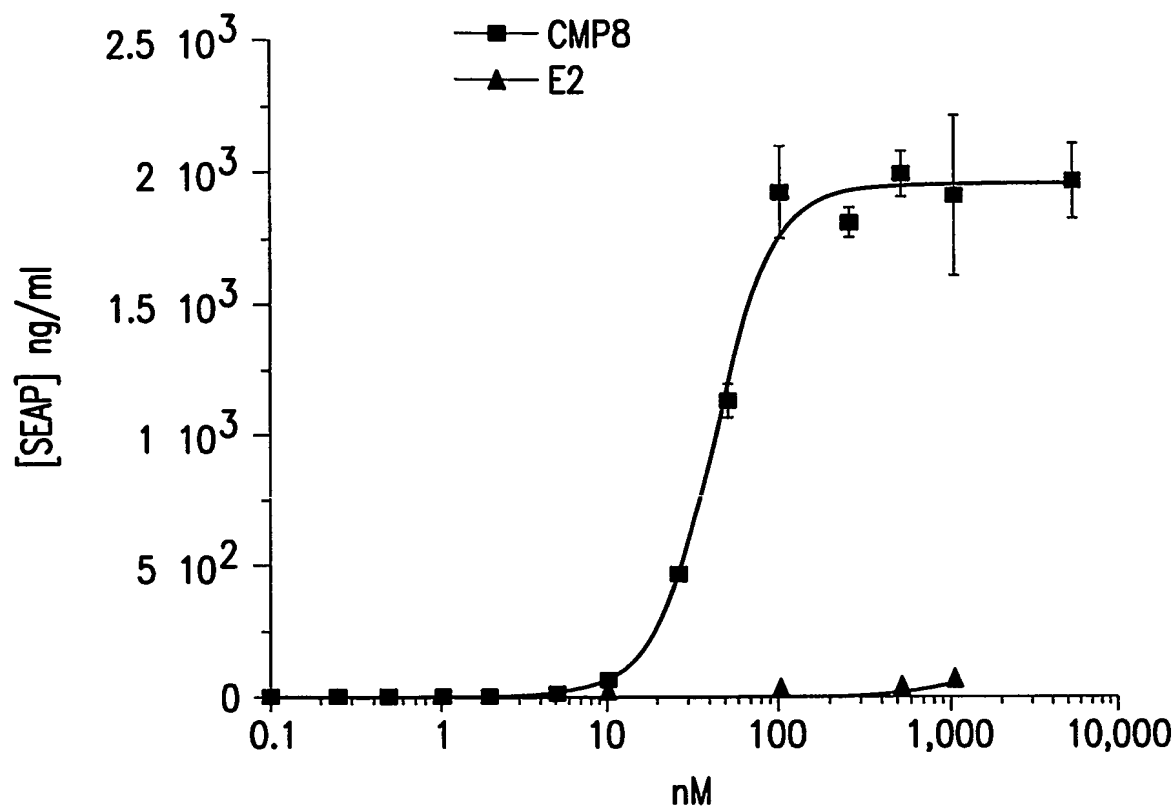


FIG.9A

| COMPOUND | EC ₅₀ (nM) |
|----------|-----------------------|
| CMP6 | 11 (±3) |
| CMP8 | 41 (±2) |
| CMP9 | 294 (±40) |
| CMP10 | 14 (±2) |

FIG.9B